UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/543,040	08/17/2006	Ali Hemmati Brivanlou	13794-105004	9176

65989 7590 03/10/2008

KING & SPALDING
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036-4003

EXAMINER	
MONTANARI, DAVID A	
ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
03/10/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

usptomailnyc@kslaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/543,040	BRIVANLOU ET AL.	
	Examiner	Art Unit	
	DAVID MONTANARI	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *1-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 July 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group 175 (anti-TMEFF1 antibody) in the reply filed on 1/11/2008 is acknowledged. The traversal is on the ground(s) that the special technical feature, though known at the time of filing, does contribute over the prior art. Applicant continues that they are the first to discover that TMEFF1 modulates TGFbeta signaling and would therefore be useful in the methods encompassed by the instant claims. Applicants continue that Groups 187-189 appear to repeat as the Groups 175-177. This is not found persuasive because while Applicant has discovered a novel use for TMEFF1 in relation to TGFbeta signaling, TMEFF1 function was known to play some role in mesodermal and endodermal formation during mouse and Xenopus development. TMEFF1 interaction with TGFbeta is not a claim limitation, whereas the elected claims 14-17 drawn to an anti-antibody towards TMEFF1 used in a method of differentiation of stem cells is what is being examined. There would be a significant search burden on the Examiner to search not only other methods of inhibiting TMEFF1 in stem cells with either anti-sense or dsRNA but the other methods which include methods of diagnosis and methods of treatment, all which would require materially distinct and separate protocols to make, use or practice.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/11/2008.

Claim Objections

The claims are objected to as reading on non-elected subject matter. Specifically the anti-TMEFF1 antibody in claim 17 encompasses any species of antibody from any mammal. However the elected invention is a human anti-TMEFF1 antibody. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue" (In re Wands, 858 F.2d 731, 737,

8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

The breadth of the claims encompasses differentiating any mammalian stem cell at any concentration and for any period of time with an anti-TMEFF1 antibody. The claimed method currently has several inoperable embodiments.

Whereas the nature of the invention is a method of differentiation involving an antibody towards TMEFF1, the art would teach that such a method would be unpredictable.

There are several significant issues with the claimed method. Firstly, is the issue that the claimed method encompasses differentiating any stem cell into endodermal or mesodermal cell types. This would include adult stem cells, which do not differentiate into endodermal or mesodermal cell types. The art teaches that only embryonic stem cells are capable of differentiating into either mesodermal or endodermal cell types (see the included handouts from http://stemcells.nih.gov/info/basics/basics3.asp and http://stemcells.nih.gov/info/basics/basics4.asp). The terms mesodermal and endodermal cell types encompass all cells within either the mesodermal and endodermal lineage, which adult stem cells may differentiate into some, only embryonic stem cells are known to differentiate into all cell types, which is encompassed by the claimed method.

A second issue with the claimed method is the "at a concentration" and "for a period of time sufficient" phrases in claim 14. The specification provides no examples nor any guidance to

the skilled artisan as to what concentration the anti-TMEFF1 antibody is to be used at nor any guidance for how long the anti-TMEFF1 antibody is to be used for. The term "sufficient" is significantly open-ended and open to interpretation by the skilled artisan and is intrinsically linked to the concentration of the antibody used in the claimed method. If the skilled artisan, for example, were to used ten times the amount of anti-TMEFF1 antibody compared to another skilled artisan, the sufficient amount of time would most likely change for differentiation. However, there is again no guidance in the specification as to what amounts of antibody or amount of time for incubation with said antibody to adequately enable the skilled artisan to practice the claimed method with a predictable degree of success.

The working examples provided in the specification teach the construction of TMEFF1 mutants (pg. 78 Example 6.2), the inhibition of nodal but not activin by TMEFF1 in two-cell stage embryos (pg. 79 Example 6.3), overexpression of TMEFF1 in early Xenopus embryos (pg. 82, parag. 0267) and a profile of TMEFF1 expression during early Xenopus development (pg. 82, parag. 0268). However the specification has failed to teach any anti-TMEFF1 antibody that would differentiate any stem cell. Further the specification has failed to teach a concentration or concentration range to use said antibody with any predictable degree of success that stem cells used in the claimed method would differentiate into mesodermal or endodermal cell types. Similarly this issue would exist for the sufficient time required to incubate the anti-TMEFF1 antibody. The claimed method presents several significant issues as detailed above that would require and undue amount of experimentation without a predictable degree of success to make and use the claimed invention.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DAVID MONTANARI whose telephone number is (571)272-3108. The examiner can normally be reached on M-Tr 8-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 1-571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

David A. Montanari, Ph.D
AU 1632

/Anne-Marie Falk/
Primary Examiner, Art Unit 1632